ataxia with oculomotor apraxia

Ataxia with oculomotor apraxia is a condition characterized by progressive problems with movement. The hallmark of this condition is difficulty coordinating movements (ataxia), which is often the first symptom. Most affected people also have oculomotor apraxia, which makes it difficult to move their eyes side-to-side. People with oculomotor apraxia have to turn their head to see things in their side (peripheral) vision.

There are multiple types of ataxia with oculomotor apraxia. The types are very similar but are caused by mutations in different genes. The two most common types (types 1 and 2) share features, in addition to ataxia and oculomotor apraxia, that include involuntary jerking movements (chorea), muscle twitches (myoclonus), and disturbances in nerve function (neuropathy). In type 1, ataxia beings around age 4; in type 2, ataxia begins around age 15. Chorea and myoclonus tend to disappear gradually in type 1; these movement problems persist throughout life in type 2. Individuals with type 1 often develop wasting (atrophy) in their hands and feet, which further impairs movement. Nearly all individuals with ataxia with oculomotor apraxia develop neuropathy, which leads to absent reflexes and weakness. Neuropathy causes many individuals with this condition to require wheelchair assistance, typically 10 to 15 years after the start of movement problems. Intelligence is usually not affected by this condition, but some people have intellectual disability.

People with ataxia with oculomotor apraxia type 1 tend to have decreased amounts of a protein called albumin, which transports molecules in the blood. This decrease in albumin likely causes an increase in the amount of cholesterol circulating in the bloodstream. Increased cholesterol levels may raise a person's risk of developing heart disease. People with ataxia with oculomotor apraxia type 2 have increased blood cholesterol, but they have normal albumin levels. Individuals with type 2 tend to have high amounts of a protein called alpha-fetoprotein (AFP) in their blood. (An increase in the level of this protein is normally seen in the bloodstream of pregnant women.) Affected individuals may also have high amounts of a protein called creatine phosphokinase (CPK) in their blood. This protein is found mainly in muscle tissue. The effect of abnormally high levels of AFP or CPK in people with ataxia with oculomotor apraxia type 2 is unknown.

Frequency

Ataxia with oculomotor apraxia is a rare condition. Type 1 is a common form of ataxia in Portugal and Japan. Type 2 is estimated to occur in 1 in 900,000 individuals worldwide.

Genetic Changes

Mutations in the *APTX* and *SETX* genes cause ataxia with oculomotor apraxia types 1 and 2, respectively. These genes provide instructions for making proteins that are involved in DNA repair.

Mutations in the *APTX* or *SETX* gene decrease the amount of functional protein that is available to repair damaged DNA, which leads to the accumulation of breaks in DNA. These breaks can be caused by natural and medical radiation or other environmental exposures, and also occur when chromosomes exchange genetic material in preparation for cell division. DNA damage that is not repaired causes the cell to be unstable and can lead to cell death. It is thought that nerve cells in the brain are particularly affected by cell death because these cells do not copy (replicate) themselves to replace cells that have been lost. The part of the brain involved in coordinating movements (the cerebellum) is especially affected. It is thought that the loss of brain cells in the cerebellum causes the movement problems characteristic of ataxia with oculomotor apraxia.

Mutations in other genes are responsible for the rare types of ataxia with oculomotor apraxia.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- adult onset ataxia with oculomotor apraxia
- EAOH
- early-onset ataxia with ocular motor apraxia and hypoalbuminemia
- SCAN2
- SCAR1
- spinocerebellar ataxia with axonal neuropathy type 2
- spinocerebellar ataxia, recessive, non-Friedreich type 1

Diagnosis & Management

These resources address the diagnosis or management of ataxia with oculomotor apraxia:

- GeneReview: Ataxia with Oculomotor Apraxia Type 1
  https://www.ncbi.nlm.nih.gov/books/NBK1456
- GeneReview: Ataxia with Oculomotor Apraxia Type 2
  https://www.ncbi.nlm.nih.gov/books/NBK1154
- Genetic Testing Registry: Adult onset ataxia with oculomotor apraxia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859598/
- Genetic Testing Registry: Ataxia-oculomotor apraxia 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3554690/
- Genetic Testing Registry: Ataxia-oculomotor apraxia 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/CN228595/
- Genetic Testing Registry: Spinocerebellar ataxia autosomal recessive 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853761/
- MedlinePlus Encyclopedia: Apraxia
  https://medlineplus.gov/ency/article/007472.htm

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Apraxia
  https://medlineplus.gov/ency/article/007472.htm
- Health Topic: Cerebellar Disorders
  https://medlineplus.gov/cerebellardisorders.html

- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Eye Movement Disorders
  https://medlineplus.gov/eyemovementdisorders.html

Genetic and Rare Diseases Information Center

- Spinocerebellar ataxia with axonal neuropathy type 2
  https://rarediseases.info.nih.gov/diseases/12860/spinocerebellar-ataxia-with-axonal-neuropathy-type-2

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Apraxia Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Apraxia-Information-Page
- National Institute of Neurological Disorders and Stroke: Ataxias and Cerebellar or Spinocerebellar Degeneration Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Ataxias-and-Cerebellar-or-Spinocerebellar-Degeneration-Information-Page

Educational Resources

- Disease InfoSearch: Adult onset ataxia with oculomotor apraxia
  http://www.diseaseinfosearch.org/Adult+onset+ataxia+with+oculomotor+apraxia/7641
- Disease InfoSearch: Spinocerebellar ataxia autosomal recessive 1
  http://www.diseaseinfosearch.org/Spinocerebellar+ataxia+autosomal+recessive+1/6771
- Merck Manual Consumer Version: Coordination Disorders
  http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/movement-disorders/coordination-disorders
- Merck Manual Professional Version: Apraxia
  http://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/apraxia
- Orphanet: Ataxia-oculomotor apraxia type 1
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1168
- Orphanet: Spinocerebellar ataxia with axonal neuropathy type 2
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=64753
- University of Minnesota Ataxia Center
  http://www.ataxiacenter.umn.edu/aboutataxia/hereditary/oculomotor/home.html

Patient Support and Advocacy Resources

- Ataxia UK
  http://www.ataxia.org.uk/
- National Ataxia Foundation
  http://www.ataxia.org/
- National Organization for Rare Disorders (NORD): Apraxia
  https://rarediseases.org/rare-diseases/apraxia/
- University of Kansas Medical Center Resource List
  http://www.kumc.edu/gec/support/ataxia.html

GeneReviews

- Ataxia with Oculomotor Apraxia Type 1
  https://www.ncbi.nlm.nih.gov/books/NBK1456
- Ataxia with Oculomotor Apraxia Type 2
  https://www.ncbi.nlm.nih.gov/books/NBK1154

Genetic Testing Registry

- Adult onset ataxia with oculomotor apraxia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859598/
- Ataxia-oculomotor apraxia 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3554690/
- Ataxia-oculomotor apraxia 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/CN228595/
- Spinocerebellar ataxia autosomal recessive 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853761/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22ataxia+with+oculomotor+apraxia%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ataxia+with+oculomotor+apraxia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ATAXIA-OCULOMOTOR APRAXIA 3
  http://omim.org/entry/615217
- ATAXIA-OCULOMOTOR APRAXIA 4
  http://omim.org/entry/616267
- ATAXIA, EARLY-ONSET, WITH OCULOMOTOR APRAXIA AND HYPOALBUMINEMIA
  http://omim.org/entry/208920
- SPINOCEREBELLAR ATAXIA, AUTOSOMAL RECESSIVE 1
  http://omim.org/entry/606002

Sources for This Summary

- Al Tassan N, Khalil D, Shinwari J, Al Sharif L, Bavi P, Abduljaleel Z, Abu Dhaim N, Magrashi A, Bobis S, Ahmed H, Alahmed S, Bohlega S. A missense mutation in PIK3R5 gene in a family with ataxia and oculomotor apraxia. Hum Mutat. 2012 Feb;33(2):351-4. doi: 10.1002/humu.21650. Epub 2011 Dec 8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22065524
- Bras J, Alonso I, Barbot C, Costa MM, Darwent L, Orme T, Sequeiros J, Hardy J, Coutinho P, Guerreiro R. Mutations in PNKP cause recessive ataxia with oculomotor apraxia type 4. Am J Hum Genet. 2015 Mar 5;96(3):474-9. doi: 10.1016/j.ajhg.2015.01.005. Epub 2015 Feb 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25728773
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4375449/
- Criscuolo C, Chessa L, Di Giandomenico S, Mancini P, Saccà F, Grieco GS, Piane M, Barbieri F, De Michele G, Banfi S, Pierelli F, Rizzuto N, Santorelli FM, Gallosti L, Filla A, Casali C. Ataxia with oculomotor apraxia type 2: a clinical, pathologic, and genetic study. Neurology. 2006 Apr 25;66(8): 1207-10.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16636238
- Le Ber I, Bouslam N, Rivaud-Péchoux S, Guimarães J, Benomar A, Chamayou C, Goizet C, Moreira MC, Klur S, Yahyaoui M, Agid Y, Koenig M, Stevanin G, Brice A, Dürr A. Frequency and phenotypic spectrum of ataxia with oculomotor apraxia 2: a clinical and genetic study in 18 patients. Brain. 2004 Apr;127(Pt 4):759-67. Epub 2004 Jan 21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14736755
- Le Ber I, Brice A, Dürr A. New autosomal recessive cerebellar ataxias with oculomotor apraxia. Curr Neurol Neurosci Rep. 2005 Sep;5(5):411-7. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16131425
- Le Ber I, Moreira MC, Rivaud-Péchoux S, Chamayou C, Ochsner F, Kuntzer T, Tardieu M, Saïd G, Habert MO, Demarquay G, Tannier C, Beis JM, Brice A, Koenig M, Dürr A. Cerebellar ataxia with oculomotor apraxia type 1: clinical and genetic studies. Brain. 2003 Dec;126(Pt 12):2761-72. Epub 2003 Sep 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14506070

Reviewed: April 2015
Published: February 14, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services